

In the claims

The following amendments are made with respect to the claims in the international application PCT/EP03/07744.

This listing of claims will replace all prior versions and listings of claims in this application.

1 (Currently amended). An isolated nucleic acid sequence, which encodes ~~for~~ a polypeptide with neuronal tryptophane hydroxylase activity, selected from the group of:

- a) a nucleic acid sequence with the sequence depicted in SEQ ID No: 1, SEQ ID No: 3 or SEQ ID No: 5 (~~DNA sequence from human, mouse, rat~~),
- b) a nucleic acid sequences, ~~which that~~ can be deduced from ~~the~~ a nucleic acid sequence[[s]] depicted in SEQ ID No: 1, SEQ ID No: 3 or SEQ ID No: 5 as a consequence of the degenerated genetic code,
- c) derivatives of the nucleic acid sequences depicted in SEQ ID No: 1, SEQ ID No: 3 or SEQ ID No: 5, which encode ~~for~~ polypeptides according to SEQ ID No: 2, SEQ ID No: 4 or SEQ ID No: 6 (~~amino acid sequences from human, mouse, rat~~), which display at least 80% homology at the amino acid level, wherein the biological activity of the polypeptides is not significantly reduced, and
- d) [[a]] human genomic nucleic acid sequences, which contain[s] the gene for sn-TPH and exhibit[s] polymorphisms.

2 (Currently amended). A [P]polypeptide[[,]] encoded by a nucleic acid sequence according to claim 1.

3 (Currently amended). The [P]polypeptide according to claim 2, ~~specified by~~ having the sequence depicted in SEQ ID No: 2, SEQ ID No: 4 or SEQ ID No: 6.

4 (Currently amended). A [R]recombinant nucleic acid molecule ~~containing~~ comprising a nucleic acid sequence according to claim 1 or parts of this nucleic acid sequence, wherein the nucleic acid sequence is connected in an anti-sense or sense-direction with one or several regulatory ~~signals~~ sequences.

5 (Currently amended). A [V]vector ~~containing~~ comprising a nucleic acid sequence according to claim 1 ~~or a recombinant nucleic acid molecule according to claim 4~~.

6 (Currently amended). A [R]recombinant prokaryotic or eukaryotic host organism containing at least one nucleic acid sequence according to claim 1 ~~or at least one recombinant nucleic acid molecule according to claim 4 or at least one vector according to claim 5~~.

7 (Currently amended). The [R]recombinant prokaryotic or eukaryotic host organism according to claim 6, wherein ~~this~~ the organism is a microorganism or an animal.

8 (Currently amended). Use of a polypeptide according to claim 2 or of peptide fragments thereof as an antigen for the production of specific polyclonal or monoclonal antibodies or antibody mixtures ~~directed against polypeptides according to claim 2 or 3~~.

9 (Currently amended). A [P]polyclonal or monoclonal antibody or antibody mixtures, which recognises specific polypeptides according to claim 2[[or 3]].

10 (Currently amended). A method for isolating a compound that binds to ~~the~~a polypeptide ~~according to~~ of claim 2, or of producing a pharmaceutical composition, comprising:

- (a) contacting a mammalian cell ~~which~~that expresses the polypeptide of claim 2 having sn-TPH activity with a compound;
- (b) detecting the presence of ~~the~~ a compound ~~which~~ that binds to the sn-TPH polypeptide, and
- (c) determining[[,]] whether the compound binds said sn-TPH polypeptide.

11 (Currently amended). [[A]] The method, according to claim 10, for the production of a pharmaceutical composition comprising the steps of the process according to claim 10 and the subsequent step of formulating the compound identified in step (c) and/or its pharmaceutically acceptable salts in a pharmaceutically acceptable form.

12 (Currently amended). A method for the treatment of a neuronal disease[s], in a patient, wherein said method is characterised in that ~~the~~serotonin production in the patient is increased or decreased by affecting the snTPH-activity.

13 (Currently amended). The [M]method for the treatment of a neuronal disease[s] according to claim 12, characterised in that the serotonin production is increased by a tissue-

specific overexpression of snTPH, by the addition of the precursor substance 5-hydroxy-tryptophane or by the addition of substituted analogues of 5-hydroxy-tryptophane.

14 (Currently amended). The [M]method for the treatment of a neuronal disease[s] according to claim 12, characterised in that the serotonin production is decreased by ribozymes, by antisense-oligonucleotides, by antisense-RNA-expression or by means of a specific TPH-inhibitors like p-chlorophenylalanine or p-ethinylphenylalanine.

15 (currently amended). A method for determining the pharmacogenetic properties of a pharmaceutically active compound and/or improving treatment of a disease, comprising a) administering the compound to a mammal, b) determining the level of expression of snTPH in a biological sample obtained from said mammal, and c) comparing said level of expression of snTPH with a level obtained from a control sample.

16 (Currently amended). The [[M]]method, according to claim 15, for the improved treatment of a disease, comprising performing the method of claim 15, and increasing or decreasing the doses of the pharmaceutically active compound to be applied to said patient.

17 (Currently amended). The [M]method according to claim 16, wherein the disease is selected from the group consisting of neuronal diseases, ~~such as~~ sleep disturbances, anxiety, alcoholism, drug abuse, disorders of food uptake ~~and/or~~ and sexual disorders.

18 (Currently amended). ~~Use of a sequence according to claim 1 or of a protein according to claim 2 or 3~~ A method for the treatment of sleep disturbances, anxiety, alcoholism, drug abuse, disorders of food uptake or sexual disorders, characterised in that the serotonin level is affected by modulating the gene expression of snTPH wherein said method comprises administering, to a patient in need of such treatment, a nucleotide sequence of claim 1 or a polypeptide of claim 2.

19 (Original). A method for diagnosing a neuronal disease, characterised in that a specific inhibition of the peripheral serotonin biosynthesis is accomplished, followed by subsequently detecting the metabolite concentrations stemming from the CNS and by determining the severity of the disease via a comparative graph.

20 (Currently amended). Use of a nucleic acid sequence according to claim 1, ~~of a recombinant nucleic acid molecule according to claim 4 or of a polypeptide according to claim 2 or 3~~ for wherein said use is selected from the group consisting of: identifying/discovering proteins, which have specific binding affinities for a polypeptide according to claim 2 or for identifying nucleic acids, which encode for proteins having specific binding affinities for a polypeptide according to claim 2 [[or 3]]; the isolation of a genomic sequence by means of homology screening or as a marker for human hereditary diseasees; and gene therapy.

21 (Currently amended). ~~Use~~The method, according to claim 20, characterised in that the Two-Hybrid-System is employed.

22 (Canceled).

23 (Canceled).

24 (Currently amended). Use of a DNA[[-]]sequence according to claim 1 or of a polypeptide according to claim 2 [[or 3]] for affecting the serotonin level via specific regulation of the snTPH-activity/amount.

25 (Currently amended). A[C]combination therapeutic comprising a polypeptide according to claim 2 ~~or 3~~ and at least one additional protein, in particular for the regulation of the serotonin metabolism.

26 (Currently amended). The[C]combination therapeutic according to claim 25, characterised in that the additional protein is a peripheral tryptophane hydroxylase.

27 (Currently amended). The[C]combination therapeutic according to claim 26, characterised in that the peripheral and the neuronal serotonin production are simultaneously increased or decreased.

28 (Currently amended). Use of the combination therapeutic according to ~~any of claims 25 to 27~~ claim 25 for the treatment of bleeding episodes in the psycho-pharmacological treatment of depressions with antidepressants, which affect the serotonin reuptake-transporter, containing antidepressants and von Willebrand-factor.